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ACUTE INHALATION EXPOSURE IN MALE ALBINO RATS		
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TOLUENE DIISOCYANATE (1321-38-6)		

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SPONSOR: The Carwin Company

MATERIALS: PAPI
MDI
TDI

SUBJECT: Inhalation Exposure
Male Albino Rats.

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203-006

I. SYNOPSIS

Male albino rats were exposed continuously for an 8-hour period to the vapors of PAPI, MDI or TDI. The concentrations in the test chamber for the test substances were found to be 0.32, 0.25 or 0.047 ppm., respectively.

All animals survived the exposure period and the 14-day observation period following exposure.

No mathematically significant alterations were observed in group body weights during the period of the test for any of the rats exposed to the respective compounds.

No meaningful pharmacotoxic signs were observed during the exposure period or during the subsequent observation period among any of the rats exposed to the compounds in this test.

No gross lesions were observed at necropsy among any of the rats sacrificed either within 24 to 48 hours after exposure or at 14 days after exposure which could be related to either of the 3 compounds used in this experiment.

The results of this test indicate that at 105° Centigrade, the vapors escaping from PAPI, TDI or MDI are not harmful to rats when exposed in the manner described in this report.

II. MATERIALS

The test compounds were received from the Carwin Company, North Haven, Connecticut as indicated below:

PAPI was received on April 14, 1964. It was a dark viscous liquid in glass bottles identified as "PAPI"; (Polymethylene Polyphenylisocyanate); Source: 01-403-0823; I. E.: 132.4; Visc: 249; % Cl: 0.30".

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TDI was received on April 14, 1964. It was a light straw-colored volatile oily liquid in a glass bottle identified as "TDI".

MDI was received on August 24, 1964. It was an orange-colored hygroscopic crystalline mass in a glass bottle identified as "MDI (pure, distilled)".

For the purpose of this study, all materials were considered to be free of impurities and were used as received.

III. METHODS

A. GENERAL PROCEDURE:

Thirty male albino Charles River rats, weighing 205 to 299 grams, were used in this study. The animals were divided into three groups of 10 rats each.

Each group of rats was exposed continuously for a single period of 8 hours to an atmosphere containing vapors of either TDI, PAPI, or MDI. Samples of the exposure chamber atmosphere were periodically obtained for analysis.

Individual body weight measurements were obtained for all rats initially, and again for surviving rats at 7 and 14 days. During the 8-hour exposure periods, all rats were observed continuously for changes in behavior or appearance. Following each exposure, the animals were examined closely for pharmacodynamic and/or toxic signs. In addition, all surviving animals were observed daily for a period of 14 days.

At 24 or 48 hours after the exposure, one-half of the rats in each group were sacrificed by means of an intraperitoneal injection of 5 per cent sodium pentobarbital and subjected to necropsy

examination. The remaining rats were similarly sacrificed and necropsied after the 14-day period of observation.

B. COMPOUND ADMINISTRATION:

Exposures were made by bubbling clean, dried, air through the respective compounds at an airflow of 2 liters per minute. Each test compound was contained in a 25 x 150 mm. tube immersed in an oil bath kept at 105° F. The airflow was then directed into an 18-liter exposure chamber containing the test animals.

C. ANALYTICAL METHODS:

A modification of the Dimethylaminobenzaldehyde method for the atmospheric determination of Toluene Diisocyanate was used to analyze the chamber air from each of the test compounds.

Samples were collected by absorption in a gas washing bottle containing 100 ml. of the reagent (0.5 per cent dimethylaminobenzaldehyde in 50 per cent glacial acetic acid). Sampling was at the rate of 2 liters per minute; length of sampling time was dependent on color development. After 2-1/2 hours the concentration was read on a spectrophotometer at 425 millimicrons using a reagent blank.

IV. RESULTS

A. BEHAVIOR, APPEARANCE, AND MORTALITY:

1. PAPI:

The group of rats exposed for an 8-hour period to an atmosphere containing PAPI vapors appeared essentially normal throughout the exposure period and the 14-day period of observation which followed. All rats survived until necropsy.

2. TDI:

Slight-to-moderate erythema was seen after 1-1/4 hours of exposure among all of the rats, which continued to the end of the 8-hour exposure period. No other signs were seen during the exposure. Examination of the rats at the termination of the exposure revealed 2-of-10 with excess moisture around the nose and 1-of-10 with ptyalism. Eight-of-ten appeared essentially normal.

All rats survived and appeared essentially normal throughout the 14-day post-exposure observation period.

3. MDI:

After one hour of exposure to an atmosphere containing MDI vapors, the group of rats exhibited signs of slight irritation, which included increased grooming activity, chewing and swallowing motions, and slight escape behavior. Inspection of the rats immediately after exposure revealed 4-of-10 with slight nasal porphyrin discharge and 2-of-10 with moisture around the nose. Six-of-ten appeared essentially normal.

The day following the exposure, slight nasal porphyrin discharge remained in 3-of-10 rats. All 10 rats survived and appeared essentially normal throughout the remaining 13 days of the observation period.

B. BODY WEIGHTS (Table 1):

Among the rats exposed to PAPI vapors, 4-of-5 showed a less than normal body weight gain over the 2-week observation period.

Body weight gains were essentially normal for the surviving rats that were exposed to TDI and MDI vapors.

Comparisons of body weight gains were made to accumulated control values obtained from rats of the same age and strain maintained in this laboratory from time-to-time.

C. NECROPSY FINDINGS:

1. PAPI:

Among the 5 rats sacrificed the day following the exposure, 1-of-5 showed no gross lesions, and 4-of-5 showed from one-to-several 1-3 mm. dark areas in the lungs. The 5 rats necropsied 2 weeks after the exposure period showed: 2-of-5 with no gross lesions; 2-of-5 with one-to-several 1-2 mm. dark areas in lungs; and 2-of-5 with several 1-4 mm. gray areas in the lungs.

2. TDI:

Necropsy of 5 rats 2 days following exposure to TDI vapors showed: 2-of-5 with no gross lesions; 3-of-5 with several 1-3 mm. dark areas throughout the lungs; and 1-of-5 with pneumonia. Gross lesions observed in the 5 rats sacrificed 2 weeks after the exposure period included: 2-of-5 with no gross lesions; 1-of-5 with several 1-3 mm. dark raised areas throughout the lungs; 1-of-5 with slight pneumonia; and 1-of-5 with several 1 mm. gray raised areas on diaphragmatic lobes of the lungs.

3. MDI:

Gross lesions observed in the 5 rats that were sacrificed the day following exposure to MDI vapors included: 1-of-5 with no gross lesions; and 4-of-5 with several 0.5-to-3 mm. dark areas throughout the lungs. The 5 rats that were necropsied 14 days after the exposure exhibited: 2-of-5 with 2-3 mm. dark red areas in the lungs; 2-of-5 with 2-3 mm. areas of alopecia on the back; 1-of-5 with several 1-2 mm. grayish areas throughout the lungs; and 1-of-5 with 2 cm. areas of ceruminous exudate in the lung lobes.

D. ANALYSES OF CHAMBER ATMOSPHERE:

Analysis of the test chamber atmosphere at 3 separate intervals during the 8-hour exposure period yielded the following results:

PAPI:	0.32 ppm.
TDI :	0.25 ppm.
MDI :	0.047 ppm.

PAPI, MDI and TDI: Acute Inhalation Exposure in Male Albino Rats.

TABLE 1. Individual Body Weights, Grams.

Animal No.	Control Weight	<u>Weeks After Exposure</u>	
		1	2
<u>PAPI:</u>			
1	252	}	Sacrificed 2 days after exposure.
2	275		
3	252		
4	207		
5	244		
6	250	258	260
7	260	254	290
8	265	267	280
9	290	283	310
10	299	304	360
<u>MDI:</u>			
11	226	}	Sacrificed 1 day after exposure.
12	270		
13	255		
14	240		
15	298		
16	265	292	340
17	245	232	225
18	225	242	285
19	235	257	285
20	245	276	315
<u>TDI:</u>			
21	209	}	Sacrificed 1 day after exposure.
22	271		
23	260		
24	228		
25	261		
26	231	310	350
27	205	219	240
28	235	258	300
29	250	276	305
30	215	257	300

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